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(54) Use of a Ginkgo Extract against Metastases

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PATENT ABSTRACTS OF JAPAN, VOL. 13, NO. 233, (C-601) (3581), MAY 29, 1989; & JP-A-1 042 426 (DAICEL CHEM. IND. LTD)
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[printer information]

CHEM. PHARM. BULL. VOL. 37, NO. 6, JUNE 1989, PAGES 1619 – 1621; PHARMAC. SOCIETY OF JAPAN H. ITOKAWA ET AL. "PAGE 1619, COLUMN 1 – COLUMN 1, LINE 3"	
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Description

Column 1

The invention relates to the use of a dry extract from ginkgo biloba leaves.

Under the tradename "Tebonin" the Dr. Willmar Schwabe is bringing a natural substance preparation to the market as an injection and infusion solution and in fact against cerebral and peripheral blood flow insufficiency and nutritive insufficiency. With this medicament in the case of post-traumatic syndrome, the symptoms of dizziness, ringing in the ears, and above all vascular-related headaches and disturbances of vision are improved. In the case of vascular-related inner ear hardness of hearing the medicament acts on the impaired hearing capability and the understanding of speech. Awareness and concentration are supposed to be increased as well as intellectual capability. States of anxiety, depressive moods, and neurological disturbances are improved.

The prior medicament has been used, i. a., in the form of infusion ampules, where one infusion ampule contains 25 ml of Extracta ginkgo bilobae e folibus siccum purissimum per injection 87.5 mg standardized to 21.0 mg ginkgoflavonglycosides.

The invention consists of the use of a dry extract from ginkgo biloba leaves for the treatment of metastatic cancerous diseases. Furthermore, the present invention consists of the use of the dry extract from ginkgo biloba leaves for infusion of 7, 17.5, or 87.5 mg or a multiple of the dose of said dry extract standardized to 1.68, 4.2, and 21.0 mg, or a multiple dose of ginkgoflavonglycosides in extract.

In so doing, it is advantageous if said dry extract is administered as a preinfusion before the dose of cytostatic chemotherapeutic agents and, in some cases, as accompanying therapy orally or parenterally.

It has been shown that chemotherapeutic agents in connection with ginkgoflavonglycosides show a greater cancer growth-inhibiting effect than the combined application of various cytostatic agents alone. The dosage of the cytostatic chemotherapy in monochemotherapy as well as in combined chemotherapy can thus be reduced with the use of C extracts. Still greater effectiveness or potentiation of the cancer growth-inhibiting effect can be achieved by multiple preinfusions of ginkgo extract with fractional low dosage of chemotherapeutic agents.

Moreover, the result can be derived according to which ginkgo extracts cause a potentiating effect in the cancer growth-inhibiting effect of various cytostatic agents.

The main problem in tumor therapy with cytostatic agents is the lack of selectivity for the tumor tissue. The maximum possible dosage is thus limited independently of the therapeutic effect due to the damaging effect on other organs – especially the blood-forming organ.

Ginkgo biloba extract (GBE) is an extract from dried leaves of the Ginkgo biloba tree. It contains, i. a., terpenes such as ginkgolides, bilobalides, flavonheterosides, and proanthocyanidine. GBE develops an effect on hemodynamics, rheology, and energetic cell metabolism.

Ginkgo biloba has the property of trapping so-called oxygen free radicals. Since the cell-destroying effect of the chemotherapy is accompanied by an increased production of free radicals, the property of trapping free radicals, especially in the better perfused areas of the stream, could explain at least a reduction of undesired effects of the chemotherapy.

Ginkgo biloba extract can antagonize effects of the platelet-activating factor (PAF). PAF is the body's own substance which seems to play a decisive role in a variety of physiological processes. Along with its blood platelet-activating function (thus the name), PAF plays a decisive role as irritation mediator. An influence of PAF on the immune system is considered as certain but still not completely investigated.

Example

GBE is available, for example, for parenteral application as lyophilisate in ampules of 50 mg active substance. Shipped with it are ampules each with 3 ml solvent. Also packaged solutions of the extract can be used (for example, the aforementioned "Tebonin").

For an application the daily dose is 200 mg GBE corresponding to 4 ampules or a multiple thereof. For this, the lyophilisate of the 4 active ingredient ampules is dissolved in the accompanying solvent (each active ingredient ampule in 3 ml solvent) and infused intravenously in 250 ml isotonic sodium chloride solution over 30 minutes.

Patients with lung metastases and liver metastases were treated who have already received two cytostatic treatment cycles applied according to standard tumor-dependent therapy. In the case of, for example, mammary carcinoma patients, the additive or potentiating effect has proven itself for an Epirubincin cyclophosphamide scheme, in the case of colorectal tumors in combination of ginkgo biloba extract with Leucoverin and Fluorouracil.

In combinations of other chemotherapy protocols the same effect is to be expected.

Before the third treatment cycle the finding must be assured by computer tomography (liver metastases) or X-ray (lung metastases). In addition, the control of the blood profile and the laboratory parameters which are required in the framework of a chemotherapeutic tumor treatment is done and makes

possible the evaluation of the course of the tumor patients to be treated accordingly.

Directly before each parenteral dose of the chemotherapeutic agent in the third treatment cycle the patients received an intravenous infusion of 200 mg of GBE.

The control investigation should be done at the point in time at which the greatest therapeutic effect is to be expected. In this control investigation the same processes come into use as in the investigation before the third treatment cycle.

In connection with GBE, anthracycline and alkylating substances appear particularly effective as cytostatic chemotherapeutic agents.

Claims

[see the English translation of German claims in the original document]

Bei Kombinationen anderer Chemotherapieprotokolle ist der gleiche Effekt zu erwarten.

Vor dem dritten Behandlungszyklus muß der Befund durch Computertomographie (Lebermetastasen) oder Röntgen (Lungenmetastasen) gesichert werden. Zusätzlich erfolgt die Kontrolle des Blutbildes und der Laborparameter, die im Rahmen einer chemotherapeutischen Tumorbehandlung erforderlich sind und die Verlaufsbeurteilung der entsprechend zu behandelnden Tumorpatienten möglich macht.

Unmittelbar vor jeder parenteralen Gabe des Chemotherapeutikums im dritten Behandlungszyklus erhalten die Patienten eine intravenöse Infusion von 200 mg GBE.

Die Kontrolluntersuchung soll zu dem Zeitpunkt erfolgen, zu dem der größte therapeutische Effekt zu erwarten ist. Bei dieser Kontrolluntersuchung kommen dieselben Verfahren zur Anwendung wie bei der Untersuchung vor dem dritten Behandlungszyklus.

In Verbindung mit GBE erscheinen anthracycline und alkylierende Substanzen als zytostatische Chemotherapeutika besonders wirksam.

Patentansprüche

1. Verwendung eines Trockenextraktes aus Ginkgo-biloba-Blättern zur Herstellung eines Arzneimittels für eine therapeutische Anwendung bei metastatischen Krebserkrankungen in Kombination mit Chemotherapeutika.

2. Verwendung nach Anspruch 1 als Vorabinfusion vor der Gabe zytostatischer Chemotherapeutika.

3. Verwendung nach Anspruch 1 oder 2 als Infusion von 7, 17,5 oder 87,5 mg oder eines Vielfachen der Dosis des genannten Trockenextraktes standardisiert auf 1,68, 4,2 und 21,0 mg oder einer vielfachen Dosis von Ginkgoflavonglykosiden im Extrakt.

4. Verwendung nach Anspruch 1 oder 2 als intravenöse Infusion von Gingko biloba-Extrakt (GBE) als Lyophilisat aufgelöst in einem Lösungsmittel und vermischt mit isotonischer Kochsalzlösung.

5. Verwendung nach Anspruch 4, gekennzeichnet durch eine Tagesdosis von 200 mg GBE, aufgelöst in 12 ml Lösungsmittel und vermischt mit 250 ml isotonischer Kochsalzlösung.

Claims

1. Use of a dry extract of Ginkgo biloba leaves for the preparation of a medicament for a therapeutic application in metastatic cancerous diseases in combination with chemotherapeutic agents.

2. Use according to Claim 1 as a preinfusion before the dose of cytostatic chemotherapeutic agents.

3. Use according to Claim 1 or 2 as an infusion of 7, 17.5 or 87.5 mg or a multiple of the dose of said dry extract standardised to 1.68, 4.2 or 21.0 mg or a multiple dose of Ginkgo flavone glycosides extract.

4. Use according to Claim 1 or 2 as an intravenous infusion of Ginkgo biloba extract (GBE) dissolved as lyophilisate in a solvent and mixed with isotonic sodium chloride solution.

5. Use according to Claim 4, characterised by a daily dose of 200 mg GBE, dissolved in 12 ml of solvent and mixed with 250 ml of isotonic sodium chloride solution.

Revendications

1. Utilisation d'un extrait sec de feuilles de ginkgo bilobé pour la préparation d'un médicament pour une utilisation thérapeutique dans les maladies cancéreuses métastatiques, en combinaison avec des agents chimiothérapeutiques.

2. Utilisation selon la revendication 1, sous forme de perfusion préalable avant l'administration des agents chimiothérapeutiques cytostatiques.

3. Utilisation selon la revendication 1 ou 2, sous forme de perfusion de 7, 17,5 ou 87,5 mg ou d'un multiple de la dose dudit extrait sec normalisé à 1,68, 4,2 ou 21,0 mg ou un multiple de la dose de flavonosides de ginkgo dans l'extrait.

4. Utilisation selon la revendication 1 ou 2 en perfusion intraveineuse d'extrait de ginkgo bilobé (EGB) sous forme d'un lyophilisat dissous dans un solvant et mélangé avec une solution isotonique de chlorure de sodium.

5. Utilisation selon la revendication 4, caractérisée par une dose journalière de 200 mg d'EGB dissous dans 12 ml de solvant et mélangé avec 250 ml de solution isotonique de